

*a2* 24. The method of claim 13, wherein the enhancing agent is a purified or recombinant bacterial antigen.

*a3* 27. The method of claim 13 or 17, wherein the autoimmune disorder is selected from the group consisting of: hay fever, allergic rhinitis, and asthma.

Please add the following new claims:

*a4* 31. The method of claim 13, wherein the enhancing agent comprises at least one bacterial cell.

*a5* 32. The method of claim 13, wherein the enhancing agent is derived from a multicellular parasite.

## REMARKS

Claims 1-30 were pending in the application. Claims 25 and 26 have been cancelled without prejudice herein. Claims 31 and 32 have been added. Accordingly, claims 1-24 and 27-32 are presently pending in the application. No new matter has been added. Support for the claim amendments can be found throughout the specification and in the claims as originally filed.

## RESPONSE TO RESTRICTION REQUIREMENT

The Examiner has required restriction of the invention under 35 U.S.C. 121 to one of the following groups:

Group I. Claims 1-4, drawn to a method of diagnosing an autoimmune disease by detecting CD3, CD69, CD94 and CD161 with antibody, classified in class 435, subclass 7.1.

Group II. Claims 1-5, drawn to a method of diagnosing an autoimmune disease by detecting TCR variable regions, CD69, CD94 and CD161 with antibody, classified in class 435, subclass 7.1.

Group III. Claims 1-5, drawn to a method of diagnosing an autoimmune disease by detecting TCR variable regions, CD3, CD69, CD94 and CD161 with antibody, classified in class 435, subclass 7.1.

Group IV. Claims 1-3 and 6, drawn to a method of diagnosing an autoimmune disease by detecting CD4/CD25 + cells that are CD122 or CD132 negative, classified in class 435, subclass 4.

Group V. Claims 7 and 9, drawn to a method of diagnosing an autoimmune disease by detecting indicator T cells, classified in class 435, subclass 29.

Group VI. Claims 8, 10-11, drawn to a method of diagnosing an autoimmune disease by detecting Th1 cytokines, classified in class 43.5, subclass 7.1.

Group VII. Claims 8, 10, 12, drawn to a method of diagnosing an autoimmune disease by detecting Th2 cytokines, classified in class 435, subclass 7.1.

Group VIII. Claims 8, 10, 12, drawn to a method of diagnosing an autoimmune disease by detecting Th3 cytokines, classified in class 435, subclass 7.1.

Group IX. Claims 13-19 and 27, drawn to a method of treating autoimmune disease by administering a bacterium from the genus lactobacillus, classified in class 424, subclass 234.1.

Group X. Claims 13-18, 20-22 and 27, drawn to a method of treating autoimmune diseases by administering LPS from a bacterium, classified in class 424, subclass 234.1.

Group XI. Claims 13-18, 20, 23, 27, drawn to a method of treating autoimmune diseases by administering bacterial cell lysate, classified in class 424, subclass 234.1.

Group XII. Claims 13-18, 20, 24, 27, drawn to a method of treating autoimmune diseases by administering purified of recombinant bacterial antigens, classified in class 424, subclass 234.1.

Group XIII. Claims 13-18, 20, 25 and 27, drawn to a method of treating autoimmune diseases by administering lam, classified in class 424, subclass 234.1.

Group XIV. Claims 13-18, 20, 26-27, drawn to a method of treating autoimmune diseases by administering  $\alpha$ -galactosyceramide, classified in class 424, subclass 234.1.

Group XV. Claims 28-30, drawn to a kit with antibody, classified in class 530, subclass 387.1.

Group XVI. Claims 28-30, drawn to a kit with nucleic acid, classified in class 536, subclass 23.5.

Applicants hereby elect group XI *with traverse*. Applicants traverse the restriction requirement to the extent that groups IX-XII should be reformed as a single group containing claims 13-24, 27, and 31-32 (referred to hereinafter as "*newly formed Group I*"). Applicants grounds for traversal are set forth below.

It is respectfully submitted that Applicant has presented an allowable generic claim, claim 13, which is generic to the claims set forth in groups IX-XII proposed by the Examiner. It is Applicants' position that given the presence of claim 13, which is generic to groups IX-XII proposed by the examiner a restriction under 35 U.S.C. §121 is improper. In view of the above traversal, *Applicants hereby elect newly formed Group I, claims 13-24, 27, and 31-32*.

It is Applicants' position that while a species election may be proper among claims 13-24, 27, and 31-32 for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable, an election under 35 U.S.C. §121 is improper since the claims are linked by an allowable generic linking claim, claim 13. Claim 13 embraces methods of preventing the development of an autoimmune disorder in a subject by administering an enhancing agent to the subject, wherein the enhancing agent comprises a bacterium (claim 31) or a multicellular parasite (claim 32), or substances derived therefrom (claim 17).

If a species election is required, Applicants further provisionally elect Group XI for search purposes only. It is Applicants' understanding that the search will be extended to the remaining species upon a finding of allowability.

If a telephone conversation with applicant's agent would expedite the prosecution of the above-identified application, the examiner is urged to call applicant's agent at (617) 227-7400.

Respectfully submitted,



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**APPENDIX A**  
**VERSION SHOWING CHANGES MADE**

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1. A method of predicting the propensity of a subject to develop an autoimmune disorder, comprising measuring i) the number or level of indicator T cells or ii) the activity of the indicator cells present in the subject as determinative of the propensity of a subject to develop an autoimmune disorder.
2. A method of diagnosing an autoimmune disorder comprising, measuring i) the number or level of indicator T cells or ii) the activity of the indicator cells present in the subject in order to diagnose an autoimmune disorder.
3. A method of predicting the efficacy of treatment for an autoimmune disorder comprising, measuring i) the number or level of indicator T cells or ii) the activity of the indicator cells present in the subject as determinative of the efficacy of treatment for an autoimmune disorder.
4. The method of any of claims 1-3, wherein the number or level of indicator T cells is measured using an antibody that recognizes T and NK-T cell surface markers selected from a group consisting of: i) an antibody that recognizes CD3 in combination with an antibody that recognizes at least one of CD69, CD94, and CD161; ii) an antibody that recognizes a TCR variable gene expressed region preferentially expressed by NK-T cells in combination with an antibody that recognizes at least one of CD69, CD94, and CD161; and iii) an antibody that recognizes a TCR variable gene expressed region preferentially expressed by NK-T cells in combination with an antibody that recognizes CD3 and an antibody that recognizes at least one of CD69, CD94, and CD161.
5. The method of claim 4, wherein the antibody that recognizes a TCR variable region preferentially expressed by NK-T cells recognizes V $\alpha$ 24 and V $\beta$ 11 and J $\alpha$ Q.

6. The method of any of claims 1-3, wherein the number or level of indicator cells is measured by detecting CD4+/CD25+ T cells that are CD122 or CD132 negative.

7. A method of predicting the propensity of a subject to develop an autoimmune disorder comprising: i) determining the number or level of indicator T cells in a biological test specimen, obtained from the subject, and ii) comparing the number or level of the indicator cells from the biological specimen to the number or level of the indicator cells in a control, wherein the presence of a reduced level of the indicator cells in the test specimen relative to the control is indicative of an increased propensity for the subject to develop an autoimmune disorder, to thereby predict the propensity of a subject to develop an autoimmune disorder.

8. A method of predicting the propensity of a subject to develop an autoimmune disorder comprising:

i) contacting a biological specimen comprising indicator T cells obtained from a subject with one or more agents that stimulate cytokine production by the indicator cells, ii) determining the level of cytokines produced by the indicator cells, and iii) comparing the level of cytokines produced by the indicator cells to a control, wherein production of lower levels of cytokines by the indicator cells obtained from the subject is indicative of an increased propensity for the subject to develop an autoimmune disorder, to thereby predict the propensity of a subject to develop an autoimmune disorder.

9. A method of determining the effectiveness of treatment for of autoimmune disorder comprising:

ii) determining the number or level of indicator T cells in the biological specimen obtained from a subject undergoing treatment for an autoimmune disorder, and ii) comparing the number or level of the indicator cells from the biological specimen to the number or level of indicator cells in a sample collected from the subject prior to treatment, wherein the presence of an increased number or level of the indicator cells in

the specimen from the subject is indicative of effectiveness of the treatment, to thereby determine the effectiveness of treatment for an autoimmune disorder.

10. A method of determining the effectiveness of treatment for of autoimmune disorder comprising:

- i) contacting indicator T cells in a post treatment biological specimen obtained from a subject undergoing treatment for an autoimmune disorder with one or more agents that stimulate indicator cell cytokine production,
- ii) determining the level of cytokines produced by the indicator cells, and
- iii) comparing the level of cytokines from the post treatment biological specimen from the subject to the level cytokines in a sample collected from the subject prior to treatment, wherein the presence of an increased level of cytokines in the post treatment specimen is indicative of effectiveness of the treatment, to thereby determine the effectiveness of treatment for an autoimmune disorder.

11. The method of any of claims 1-3, wherein the cytokines are Th1 cytokines.

12. The method of any of claims 1-3, wherein the cytokines are Th2 or TH3 cytokines.

13. (Amended) A method of preventing the development of an autoimmune disorder in a subject comprising, administering an enhancing agent to the subject, wherein the enhancing agent comprises a bacterium or a multicellular parasite or a substance derived therefrom.

14. The method of claim 13, wherein the subject is known to be at risk for the development of an autoimmune disorder.

15. The method of claim 13, wherein the subject is not known to be at risk for the development of an autoimmune disorder.

16. (Amended) A method of ameliorating the symptoms of an ongoing autoimmune disorder in a subject comprising administering [an] the enhancing agent of claim 13 to the subject.

17. (Amended) The method of claim 13, wherein the enhancing agent is [a bacterium or is] a substance derived from a bacterium.

18. (Amended) The method of claim 13 or [16] 17, wherein the enhancing agent is administered orally.

19. The method of claim [18] 31, wherein the enhancing agent is a bacterium of a genus selected from the group consisting of: [from the genus] *Lactobacillus, Mycobacteria, Bordatella, Corynebacterium, Streptococcus, or Hemophilus.*

20. (Amended) The method of claim 13 or [16] 17, wherein the enhancing agent is derived from a bacterium belonging to [a] the genus [selected from the group consisting of: ] *Mycobacteria[, Bordatella, Corynebacterium, Streptococcus, or Hemophilus].*

21. (Amended) The method of claim [20] 13, wherein the enhancing agent is administered orally.

22. (Amended) The method of claim [20] 13, wherein the enhancing agent is lipopolysaccharide.

23. (Amended) The method of claim [20] 13, wherein the enhancing agent is in the form of a bacterial cell lysate.

24. (Amended) The method of claim [20] 13, wherein the enhancing agent is a purified or recombinant bacterial antigen.

27. The method of claim 13 or [16] 17, wherein the autoimmune disorder is selected from the group consisting of: hay fever, allergic rhinitis, and asthma.

28. A kit for predicting the propensity of a subject to develop an autoimmune disorder or the effectiveness of a treatment for an autoimmune disorder comprising a detection reagent selected from the group consisting of: at least one antibody which recognizes a cell surface marker on an indicator cell and a probe that recognizes a nucleic acid molecule present in an indicator cell.

29. The kit of claim 28, further comprising at least one detection reagent that recognizes a cytokine.

30. The kit of claim 28, further comprising a means for isolating peripheral blood mononuclear cells.

31. (New) The method of claim 13, wherein the enhancing agent comprises at least one bacterial cell.

32. (New) The method of claim 13, wherein the enhancing agent is derived from a multicellular parasite.